Obesity: A Risk Factor for COVID-19

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Sukanya Srivastava, Richa Rathor, Somnath Singh, Bhuvnesh Kumar, and Geetha Suryakumar

Abstract

Introduction: Emerging data have demonstrated increased mortality of COVID-19 patients suffering from comorbid conditions such as Type II diabetes, hypertension, and cardiovascular diseases. Underlying risk in all these patients is an increase in bodyweight or obesity. The adverse health effects of obesity and how these factors enhance the risk of mortality in COVID-19 patients is still unexplored.

Objective: The enhanced fat deposition might be a risk factor for increased mortality in COVID-19 patients.

Method: We have reviewed and collected the information from online databases: Pubmed, Google scholar, Researchgate, to highlight the systematic link between obesity with associated risks in COVID-19.

Result: We have reported the first study during the pandemic from France and New York, to a currently reported study in Mexico and found individuals with BMI ≥35 kg/m^2 or >40 kg/m^2 have greater risk of developing critical illness due to COVID-19, thereby increasing mortality.

Conclusion: Our study suggests obesity in childhood, adolescence, and adulthood can be considered a profound risk factor for greater susceptibility and severity of COVID-19 and is associated with nutritional, lifestyle, cardiac, respiratory, renal, and immunological alterations, which may potentiate the complications of SARS-CoV-2 infection. Further suggesting to check on BMI during this pandemic situation.

Keywords

Obesity · COVID-19 · Inflammation · Immune dysregulation

Abbreviations

COVID-19	Coronavirus Disease 19
kg/m^2	kilogram per meter square
WHO	World Health Organization
BMI	Body Mass Index
SARS-CoV	Severe Acute Respiratory Syndrome Coronavirus
MERS-CoV	Middle East Respiratory Syndrome Coronavirus
ACE2	Angiotensin-Converting Enzyme 2
MHO	Metabolically Healthy Obese
ER	Endoplasmic Reticulum

S. Srivastava · R. Rathor · S. Singh · B. Kumar · G. Suryakumar (✉)
Cellular Biochemistry Division, Defence Institute of Physiology and Allied Sciences, Delhi, India
e-mail: sgeetha@dipas.drdo.in

A. A. A. Asea, P. Kaur (eds.), *Coronavirus Therapeutics – Volume I*, Advances in Experimental Medicine and Biology 1352, https://doi.org/10.1007/978-3-030-85109-5_12

TMPRSS2	Transmembrane Protease Serine 2
HC	Hip circumference
WC	Waist circumference
WSR	Ratio of waist to height/stature
WHR	Ratio of waist to hip
SNS	Sympathetic Nervous System
RAS	Renin-Angiotensin System
RAAS	Renal- Reabsorption-Aldosterone System
ARDS	Acute Respiratory Distress Syndrome
TNF	Tumor Necrosis Factor
IL	Interlukine
NFκB	Nuclear Factor kappa-light-chain-enhancer of activated B cells
NE	Norepinephrine Levels
PRA	Plasma Renin Activity
TH1	T helper 1
IFNγ	Interferon gamma
T2D	Type 2 Diabetes
IKK-β	IkappaB kinase beta
IRS1	Insulin receptor substrate 1
FVC	Forced Vital Capacity
FEV1	Forced Expiratory Volume in One Second
IMV	Invasive Mechanical Ventilation
FRC	Functional Residual Capacity
OSAS	Obstructive Sleep Apnea Syndrome
CVD	Cardiovascular Diseases
MCP1	Monocyte Chemoattractant Protein-1
CCL	Chemokine Ligand 2
UPR	Unfolded Protein Response

12.1 Introduction

Coronavirus disease 2019 (COVID-19), which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was declared as an outbreak by Public Health Emergency of International Concern on January 30, 2020 and a global pandemic situation on March 11, 2020 by the World Health Organization.

Individuals globally are experiencing a standstill in their day-to-day life due to COVID-19 pandemic. Coronavirus Disease 19 (COVID-19) was first reported in China in late December 2019 and has caused a global pandemic situation with large number of cases worldwide. It is caused by severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) with fever, dry cough, shortness of breath, muscle and body aches as primary symptoms, and infections resulting into life threatening form of the disease.

Recent studies have reported that, globally, more than 1.9 billion adults are overweight and 650 million are obese (WHO, Obesity and Overweight). Emerging data have demonstrated that Coronavirus disease 2019 (COVID-19) and the risk of severe acute respiratory syndrome is higher in people living with pre-existing conditions of cardiovascular diseases, diabetes, hypertension. Persons with obesity around the world are at high risk of severe complications of COVID-19 by virtue of the increased risk of the chronic diseases that obesity drives. Obesity, a condition that often coexists with diabetes and hypertension is now recently linked to higher mortality even in young patients. Low grade inflammation which is associated with obesity may be one of the major factors which is responsible for the adverse effects of these patients suffering from COVID-19. It is well known that chronic inflammation in obese people can lead to an imbalance in cytokine levels and higher activation of nuclear transcription factor kappa B (Lee et al. 2013). However, among the obese, a sub-group called metabolically healthy obese (MHO) exists, which has no inflammation (Karelis et al. 2004; Geetha et al. 2011). The MHO group may have better survival rate in case of hospitalization due to the phenomenon of obesity paradox (Ades and Savage 2010).

12.2 Morphology of Coronavirus

The coronavirus has acquired its name from the crown like morphology. The size of coronavirus ranges from 26–32 kbs in length and 65–125 nm in diameter with nucleic material containing 5′ capped positive single stranded sense RNA (Shereen et al. 2020).

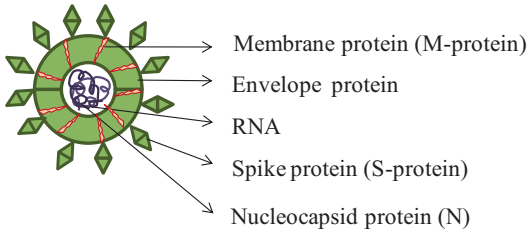


Fig. 12.1 Structure of SARS-CoV-2

As per morphology, the structure of coronavirus consists of a spike protein (S), nucleocapsid protein (N), membrane glycoprotein (M) and a lipid bilayer with an additional membrane glycoprotein (Velavan and Meyer 2020) (Fig. 12.1).

12.3 Key Features and Entry Mechanism of SARS-CoV-2

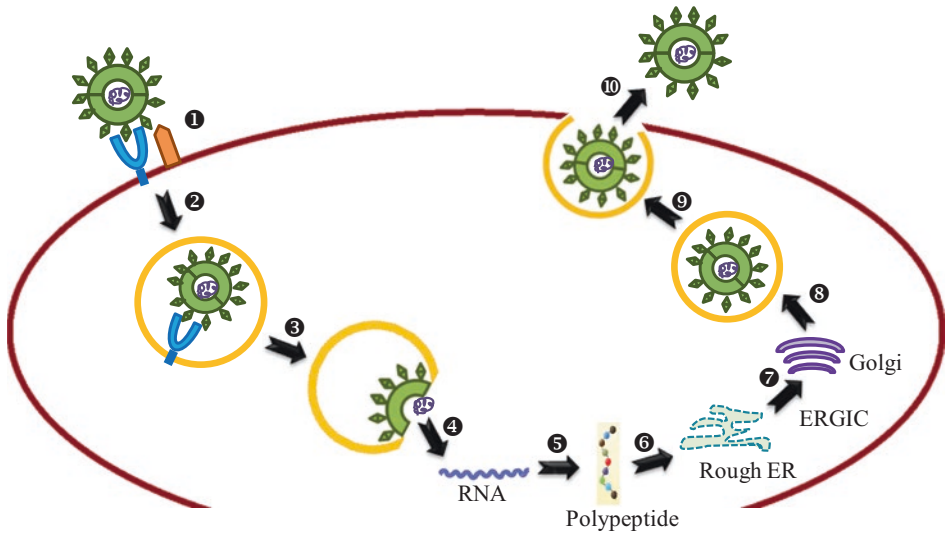
The binding of SARS-CoV-2 glycoprotein spikes (S protein) to the surface receptor, angiotensin-converting enzyme 2 (ACE2) by membrane fusion is responsible for the viral admission to the host cell (Hoffmann et al. 2020) Further, the entry of SARS-CoV-2 depends upon the cellular proteases, transmembrane protease serine 2 (TMPRSS2), which is responsible for splitting the spike S protein and promotes penetration changes (Alanagreh et al. 2020). Followed by endocytosis and release of RNA into the target cells (Shereen et al. 2020). Thereafter, the largest gene, ORF1a/b of SARS-CoV-2 encodes the pp1ab protein and 15nsps; while ORF1a gene encodes pp1a protein and 10nsps (Chen et al. 2020). The synthesized protein is further cleaved into small products via viral proteinases. Subsequently, viral proteins and genomic RNA assemble into rough endoplasmic reticulum (ER) and Golgi. Afterwards, it is transported and released out of cells via exocytosis process (Sheeren et al. 2020) (Fig. 12.2).

12.4 Symptoms

Fever is considered as initial symptom of COVID-19, later accompanied by dry cough, difficulty in breathing, dizziness, body ache, sore throat, chest pain, diarrhea, nausea, and vomit (Yi et al. 2020). Guan et al. (2020) recommends that dyspnea/hypoxemia was also experienced by some patients within one week after inception of CoV. During the initial stages of SARS, some patients are reported to develop acute respiratory distress syndrome (ARDS), accompanied by respiratory failure and other severe complications (Chen et al. 2020). The human to human transmission of this novel virus is reported to be acquired by people either by inhalation of droplets which can travel and spread up to 2 m or touching the contaminated surfaces and further touching your face, eyes, mouth or nose (Kampf et al. 2020). The binding of ACE2 with the virus might result in release of pro-inflammatory cytokines and dysfunction of multiple organs.

12.5 COVID-19 and Inflammation

Currently the attention of worldwide research is on the COVID-19 and cytokine storm. The symptomatic treatment of inflammation caused by cytokine storm, leading to respiratory dysfunction is one of the primary focuses. According to recent literature, the uncontrolled or overproduction of pro-inflammatory cytokines such as tumor necrosis factor [TNF], IL-6, IL-12 and IL-1β is known as "cytokine storm," which leads to an increase in various risk factors, including systemic inflammation, vascular hyper permeability (outflow of fluids from blood vessels), ARDS (Acute respiratory distress syndrome), multiple organ failure, and mortality if cytokine levels are persistently high (Jose and Manuel 2020). The T helper 1 (TH1) cells which are lineage of CD4+ cells and promote cell-mediated responses, secrete these pro-inflammatory cytokines, with similar mechanism observed in SARS-CoV and MERS-CoV56. Additionally, studies suggest monocytes and T lymphocytes are immune cells that are attracted by the secreted cytokine and chemokines into the infected site (Tay et al. 2020). Observations from the case studies also indicate an increase in the level of cytokines (IL1B, IL1RA, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IFN-γ, MCP1, TNFα,) and chemokines (CCL2, CCL3, CCL4, CCL5) in COVID-19-infected



❶Attachment; ❷ Entry; ❸ Fusion; ❹ Uncoating; ❺ Translation, polypeptide synthesis; ❻ & ❼ Assembly and budding; ❽&❾ Exocytosis; ❿ Viral release

: ACE2 receptor : TMPRSS2 : S protein : RNA : SARS-CoV-2

ACE2, angiotensin-converting enzyme-2; TMPRSS2, transmembrane protease serine 2; ER, endoplasmic reticulum; ERGIC, ER–Golgi intermediate compartment

Fig. 12.2 Key features and entry mechanism of SARS-CoV-2

individuals and have higher chances for being admitted to Intensive Care Units as compared to less critical patients (Huang et al. 2020). With the presence of SARS-CoV-2 in the epithelial lung cells, there is a secretion of various cytokines and chemokines from the immune cells such as: macrophages, dendritic cells, and T-lymphocytes, eventually leading to development of acute respiratory distress syndrome (Coperchini et al. 2020). More evidences suggested the association of COVID-19 with cytokine storm that causes multiple organ exhaustion, including lung and kidney dysfunction, risk of cardiovascular diseases that resulted in increased mortality rate (Nile et al. 2020). A few recent case studies reported that comorbidities such as diabetes mellitus (type 2), chronic pulmonary diseases, hypertension, and cardiovascular disease appear to increase the chances of COVID-19 infection (Caussy et al. 2020). Apart from other risks, underlying observation in many of the patients is higher Body mass Index and obesity, which is also emerging as a risk factor for severe COVID-19 infection (Dietz and Santos-Burgoa 2020) (Fig. 12.3).

12.6 Obesity

Obesity is considered as a chronic and metabolic disorder with increasing public health issue which is attributed to multiple factors like diet, hormonal, genetics as well as environment (Lee et al. 2013). Body mass index (BMI) is one of the traditional anthropometric measurements which are generally used to evaluate the degree of obesity (Mikhail et al. 1999). Body Mass Index is defined as the ratio between weight (kilogram) and height (meter square) (Center for Disease Control and Prevention, Body Mass Index). Apart from BMI, hip circumference (HC), waist circumference (WC), ratio of waist to height/stature (WSR), ratio of waist to hip (WHR), sagittal

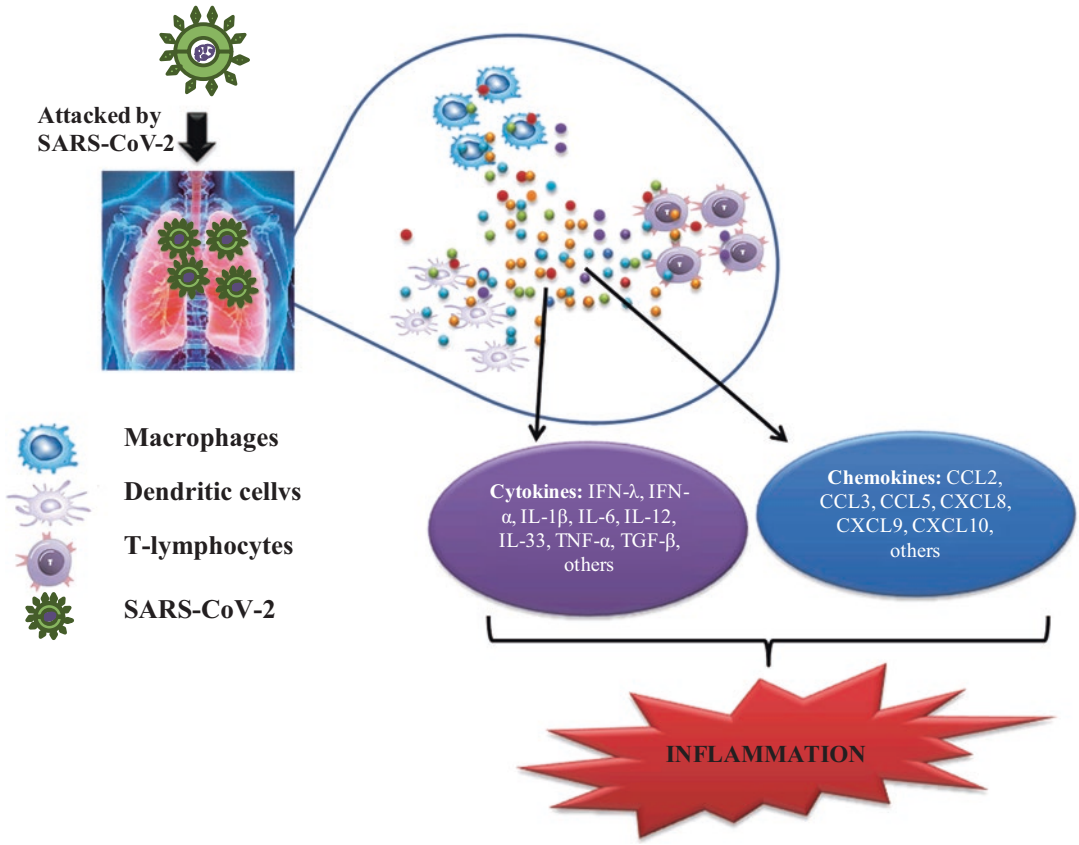


Fig. 12.3 COVID 19 infection and role of inflammation

depth, and body adiposity index are also considered as anthropometric measures, which could help in enhancing the BMI data and measures the risks related to obesity. The current classification of Body Mass Index is shown in Table 12.1.

Overweight and obesity affects multiple organs of the body, mainly heart, liver, kidney, and brain (Hall 2003). There are various life-threatening risks associated with obesity which majorly include hypertension, cardiovascular diseases, diabetes mellitus (type 2), breast cancer, infertility, and other chronic metabolic syndrome (Jiang et al. 2016).

Table 12.1 Body mass index classification of obesity

Sl. no.	Weight status	BMI (kg/m^2)	Asian population BMI (kg/m^2)
1.	Under weight	<18	<18.5
2.	Normal weight	18.5–24.9	18.5–22.9
3.	Over weight	25–29.9	23–24.9
4.	Obese	≥30	≥25
(a)	Class 1 obese	30–34.9	
(b)	Class 2 obese	35–39.9	
(c)	Class 3 obese	40.0–59.9	

WHO, Mean Body mass index

12.7 Obesity and Lifestyle

Obesity among young adults is growing rapidly all over the world due to physical inactivity, high calorie intake, and other unhealthy lifestyle habits. It is well known that obese individuals are especially vulnerable to chronic diseases such as type 2 diabetes (T2D) and cardiovascular dis-

eases. Studies have shown that genetic tendency for weight gain does not lead to obesity. The pattern of dietary intake and physical activity might play an essential role in weight gain (Jiang et al. 2016). Reports suggest young adults and adolescents are more prone to weight gain and obesity as increased calorie intake with sedentary lifestyle accompanied by change in lifestyle might incline them for becoming less active. The prolonged sedentary lifestyle can contribute to various psychological issues such as depression, insomnia, and low self-esteem further resulting into overeating and weight gain (Nestle and Jacobson 2000; Racette et al. 2005). Moreover obesity or overweight are clearly because of increase in calories intake to those utilized by the body, and excess being stored in fat tissues (Jiang et al. 2016).

12.8 Obesity and Type II Diabetes

There is a strong relationship between Body mass index, diabetes, and insulin resistance (Kahn et al. 2006). The release of various pro-inflammatory cytokines, fatty acids, glycerol in an obese individual increases the chances of insulin resistance. Being a chronic and metabolic disorder, diabetes mellitus is caused by the progressive inability to produce insulin by β-Langerhans islet cell in pancreas (Al-Goblan et al. 2014). Diabetes mellitus is categorized into two: Type I and Type II diabetes mellitus. Adipocytes (storage of energy in the form of triglycerides) and adipose tissues play an essential role in the development of insulin resistance with obesity. Studies suggest adipose tissues create adipokines such as leptin, adiponectin, retinol-binding protein-4 (RBP4), monocyte chemoattractant protein-1 (MCP-1), resistin are primarily involved in the development of insulin resistance related to obesity (Kasuga 2006). Due to chronic inflammation, there is activation of macrophage infiltration which leads to secretion of TNF-α, IL-1, IL-6, and MCP-1 and other cytokines and chemokines causing insulin resistance (Xu et al. 2003). The trigger of local inflammatory responses with secretion of various chemokines and cytokines lead to systemic insulin resistance (Kasuga 2006). The increase in the free fatty acids levels is also considered as one of the factors that are dominant in obese individuals resulting in insulin resistance as there is a decrease glucose uptake by muscles (Felber and Golay 2002). Moreover, the storage and conversion of lipid in the form of triglycerides is accumulated in both skeletal muscles as well as liver is also associated with insulin resistance. These triglycerides consist of three long chain of fatty acids and consisting acyl coenzymes A, ceramides, and diacylglycerol as metabolites which majorly contribute to impairment of both hepatic and peripheral insulin action. Hence, the process is stated as lipotoxicity (Soodini and Hamdy 2006), which is also proven to decompensate β islet cells in diabetes type 2 (Shimabukuro et al. 1998). Research evidences have also established the mRNA expression of vaspin (adipokine) in human adipose tissues and its association with obesity and insulin resistance and glucose metabolism (Klöting et al. 2006).

12.9 Obesity and Hypertension

Obesity is also associated with hypertension, which contributes to kidney-related disorders, mainly by increasing tubular reabsorption and activation of sympathetic nervous system (SNS) and RAS (renin-angiotensin system) (Jiang et al. 2016). Carbohydrate rich diet, increased consumption of alcohol, tobacco, sedentary lifestyle, and stress constitutes high risk for build-up of fat, cholesterol, and other substances on the arterial walls, hence causing restricted blood flow favoring the formation of atherosclerosis (Ross 1999). Studies have established an increased SNS activity might play an essential role in maintaining high blood pressure levels in the obese. Whereas they found in association with weight loss a decrease in plasma-renin-activity (PRA), blood pressure, and norepinephrine levels (NE) in both hypertensive and a normal obese individual (Sowers et al. 1982). Moreover, increase in sodium retention causing renal- reabsorption-aldosterone system (RAAS), the renin-angiotensin system, and increase in visceral fat stored in abdominal cavity are considered to have

primary role in hypertension related to obesity (Jiang et al. 2016). Increase in blood pressure is a result of local production of angiotensin II by various cell types, hence further increasing peripheral vascular resistance (vasoconstriction), SNS activity (Yiannikouris et al. 2012). White adipose tissues secrete a 16 kDa protein leptin having an essential role in the regulation of energy expenditure and food intake. There is an increase of plasma leptin concentration in obese individuals. Studies have also suggested, apart from obesity, leptin is also involved in complications related to cardiovascular and hypertension (Bell and Rahmouni 2016). Moreover, an influence of leptin on nitric oxide, chronic SNS activation, and sodium excretion through urine (natriuresis) might lead to sodium retention, increasing blood pressure, and vasoconstriction. Therefore, in obese individuals, leptin is also considered to play an essential role in the development of hypertension (Bravo et al. 2006).

Additionally, ACE2 (angiotensin-converting enzyme II) receptor and RAAS (renin-angiotensin-aldosterone system) are both considered as the key regulators of blood pressure. Hence the SARS-CoV 2 infection via ACE2 has shown a direct link between hypertension and COVID-19 in human cells, further resulting into severe clinical outcomes (Schiffrin et al. 2020).

12.10 Obesity and Cardiovascular Diseases

There is a direct relation between obesity and cardiovascular disorders. With increase in BMI, the chances of developing cardiovascular diseases (CVD) and coronary heart diseases are increased (Csige et al. 2018). For the cardiovascular system, the adipose tissues are often considered as crucial bioactive regulators, as they stimulate to secrete several adipokines (leptin, adiponectin, and apelin) which exert an endocrine or paracrine effect (Oikonomou and Charalambos 2019). With evidences, these adipokines are suggested to have direct and diverse effect on the myocardial metabolism, by regulating multiple cell signaling pathways (Karmazyn et al. 2008). The increase of fat deposition in adipose tissues of individuals might result in mortality and affect mobility due to cardiovascular disorders (Akil and Ahmad 2011). There is also an increased level of free fatty acids in obese individuals (Boden 2008). Due to deposition of triglycerides in their blood vessels, there is restricted blood flow in obese persons. These restricted blood vessels also accumulate toxic compounds (e.g., diacyglycerol and ceramide) over a prolonged period of time, thereby increasing the chances of programmed cell death of cardiac cells (Csige et al. 2018). This further might lead to various risk factors such as heart attack and strokes. Studies have established that buildup of abdominal fat leads to production of pro-inflammatory cytokines and adipokines, which thereby leads to major risks of cardiometabolic dysfunction such as atherosclerotic plaques (Carbone et al. 2019).

Studies suggest high frequency of pre-existing cardiovascular disease in patients suffering from COVID-19, further resulting in higher mortality. Moreover, CVDs such as arrhythmias, myocardial injury, thromboembolism, and acute coronary syndrome (ACS) have been found to be more stimulated by the SARS-CoV2. Together, these studies suggest a direct interaction between the cardiovascular system and COVID-19 (Nishiga et al. 2020).

12.11 Obesity and Respiratory Disorder

During the lack of noticeable lung disease, obese and overweight individuals have a greater chance of developing respiratory symptoms when compared to normal BMI individuals. Obstructive sleep apnea syndrome (OSAS), asthma, pulmonary embolism, and obesity hyperventilation syndrome are a few respiratory diseases which have direct association with increasing BMI and obesity (Zammit et al. 2010). There is an indirect relationship between lung volume and BMI. A decrease in lung volume is linked with increase in the BMI as well as overweight (McClean et al. 2008). With increase in BMI, longitudinal studies related to respiratory mechanics have shown a reduction in the volume of exhaled air in one sec-

ond after maximum inspiration (forced expiratory volume in 1 second—FEV1), forced vital capacity (FVC), which is forcible exhalation of the amount of air after a deep inspiration, usually measured by spirometry and functional residual capacity (FRC) (Wannamethee et al. 2005). Due to reduced physical activity during daytime, frequency of carbohydrate intake is resulting in weight gain. Hence this irregular lifestyle and increase in BMI makes an individual more inclined to develop obstructive sleep apnea. This is a very common syndrome caused by breakdown of upper airways due to which breathing cessation occurs which is repetitively nocturnal (Spicuzza et al. 2015). Evidences of reports suggest that due to exertion, obese individuals acquire symptoms like breathlessness and excessive sweating (Zammit et al. 2010). Studies observed patients with chronic cough, dyspnea, frequent smokers, or those prone to allergies have higher risk of developing asthma and COPD. In the above situation, patients are recommended to go for spirometric clinical assessment. Results indicate a decrease in the FEV1/FVC ratio (>70%) together with decrease in FEV1 and FVC levels (Poulain et al. 2006). Studies have also researched that air obstruction in dyspnea being directly associated with obesity. Moreover, obese patients having symptoms of dyspnea often are given wrong treatment without proper diagnosis and pulmonary function testing (Sin et al. 2002) a proper evaluation and diagnosis of the disease also act as a primary role for development of therapeutic strategies.

12.12 Obesity and Inflammation

Several researchers have found association of obesity with low grade systemic inflammation in which pro-inflammatory cytokines are released by activating innate immunity in the adipose tissues. Low-grade inflammation is determined by a condition of adipocyte hypoxia and dysfunction that results in an exuberant secretion of pro-inflammatory cytokines such as tumor necrosis factor α (TNF-α), interleukin (IL) 1β and IL-6 and the recruitment of immune cells macrophage, T-cell, and B-cell, creating an auto-regenerating inflammation loop. It is well reported that pro-inflammatory cytokines, such as TNF-α, IL-6 or C-reactive protein, are increased in overweight and obese adults (Muscogiuri et al. 2020)

Adipose tissues are classified as brown and white adipose tissues (Cypess et al. 2009). These tissues have adipocytes which secrete various adipokines, peptides, and pro-inflammatory cytokines such as Interleukin- 4, IFN- γ, Tumor necrosis factor α (TNF- α), Interlukine-6 (IL-6), visfatin, and resistin, which are known to exert an endocrine effect, hence communicating with other organs. Further the regulation of food intake and energy usage is controlled by these adipokines (Lafontan 2005). A hypothesis proposed by many studies suggests nutrient buildup in the adipocytes encourages cellular and metabolic stress, hence resulting in activation of various inflammatory signaling pathways (Gregor and Hotamisligil 2011). Usually folding, maturation, and storage of proteins occur in endoplasmic reticulum. Under the cellular stress induced by nutrient overload, the accumulation of misfolded proteins take place in ER, leading to activation of the UPR pathway (unfolded protein response). Furthermore, the activation of UPR pathway leads to activation of NFκB pathway (nuclear factor kappa-light-chain-enhancer of activated B cells) with increased expression of cJUX NH- terminal kinase (JNK) which is also a stress-activated protein kinase (Urano 2000) and IKK-β, IRS-1. This in turn leads to enhanced release of pro-inflammatory cytokines and induce insulin resistance (Lee et al. 2013) (Fig. 12.4).

12.13 Obesity and COVID-19

Recently adipose tissue has been recognized as an endocrine organ that secretes adipokines, which can play a major role in the metabolism as well as immune response. Altered immune response in the obese individuals may be associated with significant alteration of immune cells in the adipose tissues leading to a state of chronic inflammation both at local as well as at the systemic levels. Inflammation is at the forefront of COVID-19 research and major complications of COVID-19 infection are directly associated with

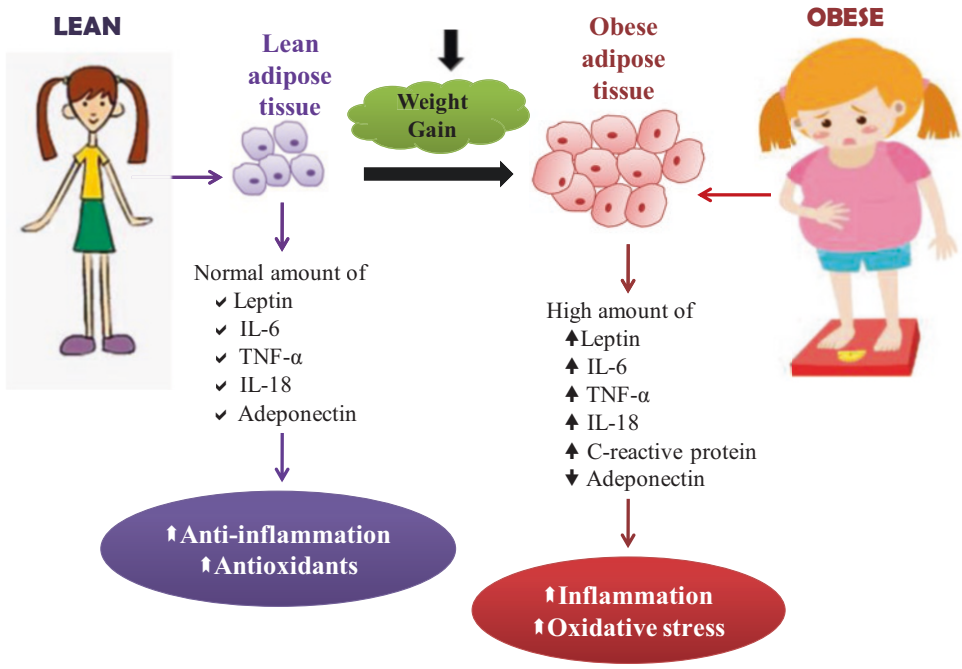


Fig. 12.4 Obesity and inflammation

systemic inflammation (Chiappetta et al. 2020; Inciardi et al. 2020).

Adipose tissue comprises a population of 3 anti-inflammatory cell types allied with normal adipose function. M-2 macrophages, T helper (Th2) cells, and regulatory T-cells (Treg) play a vital role in downstream regulation of the inflammation. Recent studies suggest adipose tissues having higher expression of ACE-2 as compared to other tissues and therefore being directly targeted by SARS-CoV-2 and SARS-CoV-2 RNA. This increased expression of ACE 2 in obese as well has been associated to the worse outcomes with COVID-19 (O'Rourke and Lumeng 2021). This increase in adipocytes in people with obesity might lead to a greater viral load as well as prolonged viremia.

Disease severity and outcome of COVID-19 patients are directly associated with dysregulation of pro-inflammatory cytokines. Increase in visceral adiposity results in obesity with low grade systemic inflammation with the pro-inflammatory cytokines by activating innate immunity in the adipose tissues. Low-grade inflammation results in an exuberant secretion of pro-inflammatory cytokines that may in some cases contribute to the "cytokine storm" of COVID-19 (Dicker et al. 2020).

Additionally, due to excessive fat, the unbalanced regulation of fatty acid metabolism, ER stress, mitochondrial dysfuncton, and hypoxia may lead to a significant alteration of cellular architecture of adipose tissues. Indeed, this favors a pro-inflammatory environment as well as maintains local and systemic inflammation in the body. Moreover people with higher BMI have impaired T and B cells' responses which causes increased vulnerability and delay in viral resolutions (Thus the inflammation ascending from COVID-19, may strengthen prevailing chronic inflammation in obese individuals and further enable viral growth and its spread leading to worst clinical outcomes (Mohammad et al. 2021). Obesity associated with comorbidities such as reduced pulmonary function, diabetes mellitus (Type 2), cardiovascular dysfunction, and hypertension may place people with obesity at high risk of the viral infection (COVID-19) and affect the overall health (Simonnet et al. 2020). Reports suggested an increase in C reactive protein (CRP) and decrease in lymphocyte count was observed in COVID-19 patients (Chen et al. 2020; Qin

et al. 2020; Zilong et al. 2020; Li et al. 2020). One of the interesting studies described that multiple types of chemokines such as G-CSF, GM-CSF, IP-10, MCP-1, MIP-1a, MIP-1b, RANTES, and IL-8 with higher level was observed in COVID-19 patients (Huang et al. 2020). Tang et al. (2020) reported the increase of IL-6 and IL-10 in COVID-19 patients. Not only this, the group also emphasized the crucial role of IL6 in the pathology of COVID-19 that results into chemotaxis of neutrophils and lymphocyte necrosis. Importantly, COVID-19 is more able to cause cytotoxic lymphocytes exhaustion.

Another important finding is obesity-induced chronic inflammation and impaired fibrinolysis which enhances the risk of thrombosis. That could be a probable mechanism potentially involved in lung injury and severe COVID-19 infection. These adverse effects are potentially involved in lung injury and severe COVID-19 infection. COVID-19 patients showed a marked increase in thrombotic complications due to hypercoagulability. Latest study described the acute lung injury in COVID-19 patients which involve fibrin deposition in the pulmonary microcirculation and formation of microthrombi (Paramo 2020). Another study reported that high fibrinogen and a high D-dimer are characteristic of patients with COVID-19 (Hayiroglu et al. 2020; Levi et al. 2020; Blasi et al. 2020).

These are the plausible mechanisms which could explain the increased risk of severe complications of COVID-19 for subjects with obesity.

The current pandemic situation of Coronavirus Disease 19 has focused worldwide research on its life-threatening risk factors. The initial data suggest, older individuals (age >60) suffering from any diabetes, cardiovascular disorders, kidney, or respiratory disorders are highly vulnerable to this viral infection. Table 12.2 describes the available data on the incidence of obesity and risk of COVID 19 fatality.

The very first report to focus on BMI data with small number of patients was conducted by Simonnet et al. 2020 from February 27 to 5 March 2020 at Lille, France and found high frequency of obesity among individuals admitted to intensive care (ICU) for COVID-19. Out of 124 patients independent of their age, sex, hypertension, and diabetes admitted in intensive care unit, 47.6% were obese (BMI > 30 kg/m^2), including class II obesity (BMI 35–39.9 kg/m^2) in 13.7% together with class III obesity (BMI ≥ 40 kg/m^2) in 14.5%.and 28.2% were under severe obesity (BMI > 35 kg/m^2). Identically, the requirement of invasive mechanical ventilation (IMV) in patients with BMI > 35 kg/m^2 was higher. Correspondingly, in New York, another study was conducted with a large number of obese adults. Researchers established a study on 3615 individuals with PCR positive cases for COVID-19 during 4 March 2020–4 April 2020 and found that 21% of individuals had BMI >35% and patients aged less than 60 are 2.0–1.8 times more potentially to be admitted to ICU with BMI between 30–34 kg/m^2 (Lighter et al. 2020). Similar study on 393 COVID positive patients in the same city was conducted in two different hospitals by Goyal et al in 2020. The author found that out of 393, 35.8% were obese during their admission at the hospital. He had also discussed about various serious symptoms, including hypertension, diabetes, COPD, asthma, as a few comorbidities in patients. Likewise, another investigation by Stefan et al. 2020 was conducted with gradually less no. of patients in Seattle region with 24 ill COVID-19 positive patients. The data indicated, among them three patients, were reported to lay under normal BMI category, whereas seven were overweight and 13 fall under obesity category. Further mechanical ventilation was required by 85% patients with obesity and 36% of the same were reported to be dead. Similarly, a study on admitted patients of COVID-19 positive was conducted in China, and they found that, out of 383 patients, 53.1% had normal weight with BMI 18.5–23.9 kg/m^2, 32.0% were found to be overweight with a BMI of 24–29.7 kg/m^2 and 10.7% were found to be obese with BMI ≥ 28 kg/m^2. Further the researchers also suggested that on comparison with non-obese patients, obese patients are more inclined to have cough and fever symptoms as well as overweight patients are 1.84-fold more likely to have severe symptoms of COVID-19 when compared with normal weight patients; however, obese individuals have

Table 12.2 The incidence of obesity and risk of COVID 19 fatality

S.no	Number of positive COVID-19 cases	Country/ city	BMI (kg/m^2)	Requirement of ventilator	Mortality	Reference
1.	124	Lille (France)	47.6% (BMI > 30 kg/m^2), 13.7% (BMI 35–39.9 kg/m^2), 28.2 (BMI > 35 kg/m^2)	68.6%		Simonnet et al. (2020)
2.	3615	New York	21% (BMI 30–34 kg/m^2), 16% (BMI ≥ 35 kg/m^2)	1.8 times 2.2–3.6 times	12%	Lighter et al. (2020)
3.	393	New York	35.8 %	43.4%	–	Goyal et al. (2020)
4.	24	Seattle	7 (Overweight) 13 (obese)	85%	36%	Stefan et al. (2020)
5.	383	China	32% (BMI 24.0–27.9 kg/m^2), 10.7% (BMI ≥ 28 kg/m^2)	3.40-fold		Cai et al. (2020)
6.	5566	New York	23.7% (BMI < 25 kg/m^2), 34.2% (BMI 25–29 kg/m^2), 32.8% (BMI 30–39 kg/m^2), 6.8% (BMI > 40 kg/m^2)	26.9% (BMI < 25 kg/m^2), 32.7% (BMI-25–29 kg/m^2), 30.7% (BMI 30–39 kg/m^2), 7.7% (BMI ≥ 40 kg/m^2)		Petrilli et al. (2020)
7.	5700	New York	41.7% (BMI ≥ 30)	12.2%	19.0 % (BMI ≥ 35)	Richardson et al. (2020)
8.	463	Detroit	57.6% 19.2% severe obese	2.0	–	Suleyman et al. (2020)
9.	51,633	Mexico	20.7%	5.0%	13.5%	Bello-Chavolla et al. (2020)

3.40-fold chances of developing severe disease (Cai et al. 2020), hence suggesting obese individuals are prone to develop this viral disease.

Gradually, after some awareness on this issue, more investigations worldwide are in process. Researchers are finding obesity to play a crucial factor in aggravating the COVID scenario. Subsequently, a large number of cohort studies was carried out in New York, which is also known to have a large number of obese adults. Petrilli et al. (2020) established a similar study in New York with larger number of patients; 5566 adults were found to be positive for COVID-19 and 2741 were needed to be admitted in hospital. Out of which, 650 (23.7%) had BMI < 25 kg/m^2, 939 (34.30%) had BMI ranging from 25–29 kg/m^2, 899 (32.8%) had a BMI between 30–39 kg/m^2, and 185 (6.8%) had a BMI > 40 kg/m^2. Whereas out of 990, 266 (26.9%) having BMI < 25 kg/m^2, 324 (32.7%) with BMI-25–29 kg/m^2, 304 (30.7%) with BMI 30–39 kg/m^2, and 70 (7.7%) having BMI ≥ 40 kg/m^2 were reported to be critically ill or in requirement of mechanical ventilator or intense critical care. Furthermore, an alternative case study in the same city was conducted among patients hospitalized with positive COVID-19, where obesity was regarded as a common comorbidity with hypertension and diabetes. Among 5700 patients, 41.7% (1737) had BMI ≥ 30 and 12.2% received Intensive mechanical ventilation, with 19.0% (BMI ≥ 35) mortality rate (Richardson et al. 2020). Recent research has also given more evidence on obesity being associated with COVID-19. A study was conducted on 463 and 50,633 hospitalized COVID-19 patients, where obesity was considered as comorbidity in Detroit and Mexico, respectively. In Detroit, 57.6% were obese and 19.2% were reported as severely obese, and severe obesity was associated with the need of intensive care admission and mechanical ventilation (Suleyman et al. 2020). Whereas in Mexico, obesity was mediated through diabetes with 20.7% obese patients, where 5% were

shifted to intensive care unit and a 13.5% mortality (Bello-Chavolla et al. 2020). Sattar et al. (2020) suggests excess fat deposition might be a unifying risk factor for COVID-19 that most likely dysregulated the immune system and reduced protective cardiorespiratory reserve, which majorly appears to be a part of this critical illness, thereby increasing mortality. Severity and vulnerability of COVID-19 in association with cardiac, nutritional alteration, and other comorbidities is not only limited to adults but also to children and adolescents being more susceptible to SARS-CoV-2 infection (Nogueira-de-Almeida et al. 2020). A new study in the medical journal The Lancet by Kass et al. (2020) reported an inverse correlation between BMI and age among 265 individuals, further suggesting the younger population with high BMI more likely to get affected by COVID-19.

India currently has the third-highest number of overweight or obese individuals among all the countries. A study on trends of overweight/obesity in India shows rise from 9% to 21% in case of women and 11% to 19% for men during the period between 2005 and 2016 (International Institute of Population Sciences 2017). On the one hand there is malnutrition in India and, on the other, the increase in overweight/obesity in the population of poor socioeconomic status may further increase vulnerability to infections as well as non-communicable diseases (Luhar et al. 2018). However, till date, no data are available on the risk of obesity and COVID 19 patient severity. Clinicians treating the disease in India have reported that a large number of COVID patients is overweight and obese and there is an urgent need to understand the link.

In conclusion, obesity in childhood and adolescence can be considered a risk factor for greater susceptibility and severity of COVID-19 and is associated with nutritional, cardiac, respiratory, renal, and immunological alterations, which may potentiate the complications of SARS-CoV-2 infection.

12.14 Lifestyle Modification in the Global Pandemic

The global pandemic has influenced and modified our lifestyle to a great extent. The lockdown imposed all over the world has a negative impact on diet, sleep, and physical activity. Maintaining a healthy lifestyle, while being isolated and safe has become the need of the hour. There are various reports in which the author has addressed the psychological impact of this pandemic situation, instead of lifestyle issues which mainly include increased screen-time, reduced physical activity, high fat diet intake (Balanzá-Martínez et al. 2020) further being inclined towards weight gaining. Being quarantined with unscheduled routine has created a monotonous lifestyle, and continuous hearing about the stressful pandemic situation might result in sleep disturbance, overeating of foods rich in fat, proteins, carbohydrates, and mostly the sugary comfort foods (Muscogiuri et al. 2020). All these activities are creating a risk factor for various health issues and chronic diseases, especially in young children and adults.

People all over the world must be encouraged to improve their lifestyle to lessen risk both in the current and subsequent waves of COVID-19. Better diet plans and sustainable lifestyle changes must be ensured so as to promote positive well-being. To ensure a healthy lifestyle, one must incorporate proper balanced diet and regular physical exercise, yoga, or meditation. The diet should include a variety of fresh fruits, vegetables, legumes, nuts, and whole grain to get the required amount of macronutrients (carbohydrates, fat, and protein), micronutrients (vitamins, water and minerals), and antioxidants. Vitamin C, vitamin E, zinc, copper, and Selenium are a few antioxidant nutrients, with fruits and vegetables as the primary source which help to prevent cell damage by free radicals, further boosting the immune system. Foods rich in probiotics and prebiotics such as yogurt, fermented,

and fibrous foods are known to support a healthy colony of microorganism in the gut and ease the bowel movement (Miller et al. 2017).

Sleep also plays an important role in maintaining a healthy lifestyle. Getting proper and quality sleep also helps in maintaining our physical, mental health. A regular sleep of 7–8 h is important to keep us healthy as it also boosts immunity.

Apart from a healthy diet, one must also include some sort of physical exercise in their schedules**.** Yoga and meditation are also considered as easy and inexpensive tools with long-term benefits on both physical health and mental condition. This being the pressing priority, it is able to improve overall fitness level, posture, and flexibility. Apart from improving physical health, yoga and meditation also clears our mind from regular stress.

12.15 Implications for Future Research

Although the risk of obesity with several chronic diseases is well known, emerging data indicate that obesity may have a link with the severity of COVID-19 infection. There is an increased prevalence of diseases such as diabetes, hypertension, cardiovascular diseases, and kidney dysfunction in obese individuals. All these conditions are major risk factors for disease severity and mortality associated with COVID-19. Hence, obesity is an additional risk factor associated with worse outcomes in COVID-19 patients. Insulin resistance is an important outcome of obesity which may play a key role in the altered immune response in the obese individuals. Hence it may be helpful if markers of insulin resistance are assessed to look at the association between insulin resistance and the severity of CoVID-19 disease. Most research data that were published about comorbid conditions, which may be associated with increased risk of severe COVID-19, did not provide data about body fat mass or metabolic health. It is imperative that data about fat mass and body composition be collected and further research be carried out. Further, it's time that we tackle and prevent obesity in our society not only for this viral pandemic but also for the prevention of various chronic diseases (Fig. 12.5).

Conflict of Interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

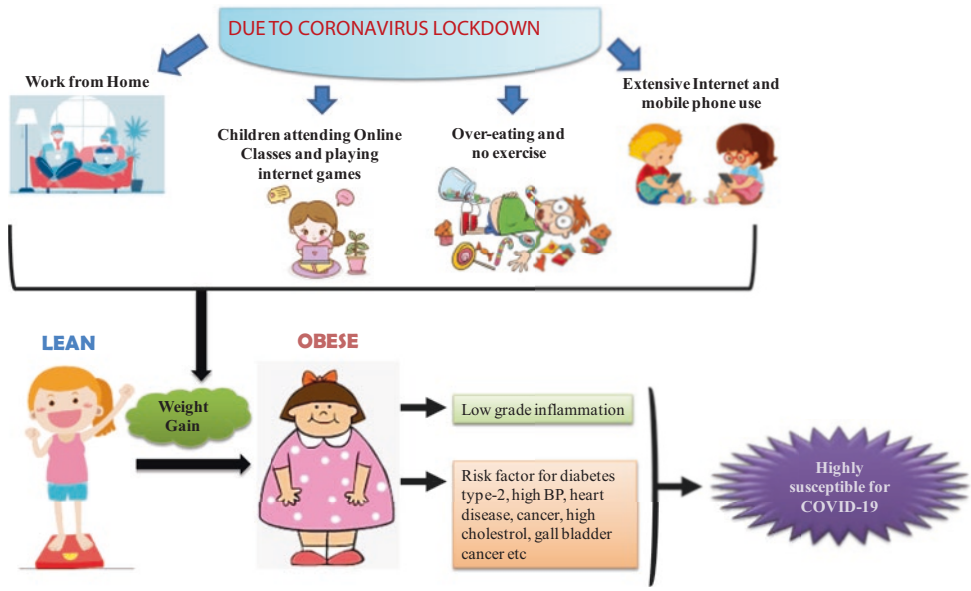


Fig. 12.5 Obesity-related comorbidities and high risk and severity of COVID-19 infection

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